

## **LISTING OF CLAIMS:**

The following listing of claims will replace all prior versions, and listing, of claims, in the subject application:

Claim 1. A method of operating a time-of-flight mass spectrometer, the spectrometer having a first region including a sample source disposed therein, and an ion detector remote from the first region, the method comprising the steps of:

establishing a non-zero field within the first region of the spectrometer;  
generating ions from the sample source within the first region;  
establishing an ion accelerating field within the first region after establishing said non-zero field therein, said ion accelerating field accelerating said ions generated within the first region toward the ion detector; and  
detecting said accelerated ions at the ion detector and determining therefrom mass to charge ratios of said accelerated ions.

Claim 2. The method of claim 1 wherein the accelerating step occurs a predetermined time period after the generating step.

Claim 3. The method of claim 2 wherein the detecting step includes the steps of:  
measuring time-of-flight of the generated ions as elapsed time between acceleration of the generated ions and arrival times of the various accelerated ions at the ion detector; and  
determining mass-to-charge ratios of the various accelerated ions from the corresponding time-of-flight measurements.

Claim 4. The method of claim 1 wherein said non-zero field is a non-zero electric field.

Claim 5. A method of operating a time-of-flight mass spectrometer to minimize deleterious effects of distributions in initial ion position and initial ion velocity on the ion mass resolution of the spectrometer, said spectrometer including a first region for generating ions from a sample source disposed therein and an ion detector remote from the first region, the method comprising the steps of:

determining an equation for the time-of-flight of said ions generated within the first region to the detector, said equation being a function of a set of ion variables including initial position distribution and initial velocity distribution of said ions generated within the first region, said equation further being a function of a set of spectrometer variables including a time delay between generation of said ions within the first region and application of an ion accelerating electric field within the first region for accelerating said ions generated therein toward the detector;

determining an optimum set of values for said spectrometer variables from said equation such that any decrease in mass resolution of the spectrometer due to effects of said ion variables thereon are minimized;

generating said ions from the sample source within the first region; and

establishing an ion accelerating electric field within the first region for accelerating said ions generated therein toward the ion detector in accordance with said optimum set of values for said spectrometer variables.

Claim 6. The method of claim 5 wherein the sample source and the detector define a distance therebetween and said ion accelerating electric field has an accelerating field strength associated therewith; and

wherein said set of spectrometer variables further includes either of the distance between the first region and the detector and the accelerating field strength.

Claim 7. The method of claim 5 further including the step of establishing a non-zero electric field within the first region prior to establishing said ion accelerating electric field therein.

Claim 8. The method of claim 7 wherein the sample source and the detector define a distance therebetween, said ion accelerating electric field has an accelerating electric field strength associated therewith, and the non-zero electric field has a non-zero electric field strength associated therewith; and

wherein said set of spectrometer variables further includes any of the distance between the first region and the detector, the accelerating electric field strength and the non-zero electric field strength.

Claim 9. The method of claim 5 wherein the ions are generated from the sample source within the first region via laser desorption.

Claim 10. The method of claim 5 wherein a derivative of said equation varies widely with respect to a range of initial ion positions and with respect to a range of initial ion velocities.

Claim 11. The method of claim 10 wherein the sample source and the detector define a distance therebetween and said ion accelerating electric field has an accelerating field strength associated therewith; and

wherein said set of spectrometer variables further includes either of the distance between the first region and the detector and the accelerating field strength.

Claim 12. The method of claim 11 further including the step of establishing a non-zero electric field within the first region prior to establishing said ion accelerating electric field therein.

Claim 13. The method of claim 1, wherein said method further comprises the step of said ions from said first region are reflected toward said ion detector.

Claim 14. The method of claim 1, wherein said sample source is a conductive metal grid.

Claim 15. The method of claim 1, wherein said sample source is a dielectric surface.

Claim 16. The method of claim 1, wherein said sample source is a dielectric surface with a thin film coating.

Claim 17. The method of claim 1, wherein said sample source is a metal surface.

Claim 18. The method of claim 1, wherein said first region is bound on one end by said sample source and on the other end by a first electrode.

Claim 19. The method of claim 1, wherein said ions generated from said sample source have an initial velocity component perpendicular to said first electrode.

Claim 20. The method of claim 1, wherein said ions generated from said sample source have an initial velocity component parallel to said first electrode.

Claim 21. The method of claim 20, wherein said ions are continuously generated from said sample source.

Claim 22. The method of claim 18, wherein said ions generated from said sample source have an initial velocity distribution within the first region.

Claim 23. The method of claim 18, wherein said first electrode is a grid.

Claim 24. The method of claim 18, wherein said first electrode is a conductive plate having at least one hole.

Claim 25. The method of claim 18, wherein said first electrode is a conductive plate having a plurality of holes.

Claim 26. The method of claim 18, wherein said first electrode comprises a groove through the center of its surface for receiving said sample source.

Claim 27. The method of claim 1, wherein said ions have a initial velocity component.

Claim 28. The method of claim 1, wherein said ions are desorbed from a surface.

Claim 29. The method of claim 1, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 30. The method of claim 1, wherein said ions have an initial velocity component perpendicular to said sample source.

Claim 31. The method of claim 1, wherein said ions have an average initial velocity component greater than zero.

Claim 32. The method of claim 1, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 33. The method of claim 1, wherein said method comprises the further step of deflecting unwanted ions from the ion path to the detector.

Claim 34. The method of claim 1, wherein said generating is fast atom bombardment.

Claim 35. The method of claim 1, wherein said generating is matrix assisted laser deposition.

Claim 36. The method of claim 1, wherein said generating is plasma desorption.

Claim 37. The method of claim 1, wherein said generating is secondary ion generation.

Claim 38. The method of claim 1, wherein said generating is electron bombardment.

Claim 39. The method of claim 1, wherein said method further comprises the step of employing an optimization method to determine optimum values for voltages applied within the first region to create the ion accelerating field.

Claim 40. The method of claim 39, wherein said optimization method is Simplex optimization.

Claim 41. The method of claim 1, wherein said ions are generated from a DNA sample.

Claim 42. The method of claim 1, wherein said ions are generated from a protein sample.

Claim 43. A time-of-flight mass spectrometer (TOFMS) for determining the mass to charge ratios of accelerated ions, wherein said TOFMS comprises:

a first region including a sample source disposed therein;  
an ion deflector remote from the first region;  
an ion detector remote from said ion deflector;  
means for establishing a first field within said first region;  
means for generating ions from said sample source;  
means for establishing a second field within said first region at a predetermined time after  
establishing said first field; and  
means for energizing said ion deflector;  
wherein said second field accelerates said ions generated within said first region towards  
said deflector; and  
wherein said deflector reflects said ions toward said detector.

Claim 44. The TOFMS according to claims 43, wherein said first field is predetermined to  
attract positively charged ions.

Claim 45. The TOFMS according to claims 43, wherein said first field is predetermined to  
attract negatively charged ions.

Claim 46. The TOFMS according to claims 43, wherein said sample source is a conductive  
metal grid.

Claim 47. The TOFMS according to claims 43, wherein said sample source is a dielectric  
surface.



Claim 48. The TOFMS according to claims 43, wherein said sample source is a dielectric surface with a thin film coating.

Claim 49. The TOFMS according to claims 43, wherein said sample source is a metal steel surface.

Claim 50. The TOFMS according to claims 43, wherein said first region is defined by a first grid juxtaposed with a second grid.

Claim 51. The TOFMS according to claims 50, wherein said TOFMS further comprises a second region defined by a third grid juxtaposed with said second grid.

Claim 52. The TOFMS according to claims 51, wherein a third field is established in said second region.

Claim 53. The TOFMS according to claims 50, wherein said ions generated from said sample source have an initial velocity component perpendicular to said second grid.

Claim 54. The TOFMS according to claims 50, wherein said ions generated from said sample source have an initial velocity distribution within said second region.

Claim 55. The TOFMS according to claims 54, wherein said ions are continuously generated from said sample source.

Claim 56. The TOFMS according to claims 50, wherein said ions generated from said sample source have a first initial velocity component perpendicular to said second grid and a second initial velocity component parallel to said second grid.

Claim 57. The TOFMS according to claims 50, wherein said second grid is a conductive plate having at least one hole.

Claim 58. The TOFMS according to claims 50, wherein said second grid is a conductive plate having a plurality of holes.

Claim 59. The TOFMS according to claims 50, wherein said first grid has a groove through the center of its surface for receiving said sample source.

Claim 60. The TOFMS according to claims 43, wherein said ions have a initial velocity component.

Claim 61. The TOFMS according to claims 43, wherein said ions are desorbed from a surface.

Claim 62. The TOFMS according to claims 43, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 63. The TOFMS according to claims 43, wherein said ions have an initial velocity component perpendicular to said sample source.

Claim 64. The TOFMS according to claims 43, wherein said ions have an average initial velocity component greater than zero.

Claim 65. The TOFMS according to claims 43, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 66. The TOFMS according to claims 43, further comprising a deflector to deflect unwanted ions from the ion path.

Claim 67. The TOFMS according to claims 43, wherein said means for generating said ions is fast atom bombardment.

Claim 68. The TOFMS according to claims 43, wherein said means for generating said ions is matrix assisted laser deposition.

Claim 69. The TOFMS according to claims 43, wherein said means for generating said ions is plasma desorption.

Claim 70. The TOFMS according to claims 43, wherein said means for generating said ions is secondary ion generation.

Claim 71. The TOFMS according to claims 43, wherein said means for generating said ions is electron bombardment.

Claim 72. The TOFMS according to claims 43, wherein an optimization method is employed to determine optimum values for the potentials and the predetermined times at which the potentials are applied to the first, second, third, and fourth grids.

Claim 73. The TOFMS according to claims 72, wherein said optimization method is Simplex optimization.

Claim 74. The TOFMS according to claims 43, wherein said ions are generated from a protein sample.

Claim 75. The TOFMS according to claims 43, wherein said ions are generated from a DNA sample.

Claim 76. A method of improving mass resolution in time-of-flight mass spectrometry, said method comprising the steps of:

applying a first potential to a sample holder;

applying a second potential to a first element spaced apart from the sample holder,

wherein said sample holder and said first element defining a first region and wherein said first and second potentials define a first electric field in said first region;

ionizing a sample proximately disposed to the holder to form sample ions;

energizing an ion deflector spaced apart from the first element; and  
applying a voltage pulser for changing the potential difference between the sample holder  
and the first element at a predetermined time which defines a second electric field between the  
sample holder and the first element to accelerate said ions from said first region toward said  
deflector;

wherein the first and second electric fields and the predetermined time are chosen such  
that a flight time of said ions from said first region toward said deflector have a mass-to-charge  
ratio that is independent to second order of initial velocity.

Claim 77. A time-of-flight mass spectrometer (TOFMS), wherein said TOFMS comprises:

a source region including a sample holder and at least one electrode disposed therein;

means for generating ions from said sample holder;

an ion deflector, said deflector being energized;

means for accelerating said ions orthogonally from said source region into a drift region of said TOFMS toward said ion deflector; and

an ion detector remote from said ion deflector for detecting said accelerated ions such that mass to charge ratios may be determined;

wherein a first potential is applied to said sample holder to accelerate said ions towards said means for accelerating;

wherein said deflector reflects said ions toward said detector; and

wherein the time spread in the time of flight of ions of a predetermined mass to charge ratio generated within said source region to the means for detecting is minimized.

Claim 78. The TOFMS according to claim 77, wherein said means for accelerating comprises a pair of electrodes.

Claim 79. The TOFMS according to claim 78, wherein said pair of electrodes comprises at least one plate and at least one grid.

Claim 80. The TOFMS according to claim 78, wherein at least one potential is applied to at least one of said electrodes such that an electric field is generated within said means for accelerating.

Claim 81. The TOFMS according to claim 78, wherein said ions generated in said source region have an initial velocity component parallel to a surface of said electrodes of said means for accelerating.

Claim 82. The TOFMS according to claim 77, wherein said ions have an initial velocity component perpendicular to said sample holder.

Claim 83. The TOFMS according to claim 77, wherein said ions are desorbed from a surface of said sample holder.

Claim 84. The TOFMS according to claim 77, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 85. The TOFMS according to claim 77, wherein said ions are continuously generated in said source region.

Claim 86. The TOFMS according to claim 77, wherein said ions have a initial velocity component.

Claim 87. The TOFMS according to claim 77, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 88. The TOFMS according to claim 77, wherein said ions have an average velocity component greater than zero.

Claim 89. The TOFMS according to claim 77, wherein said TOFMS further comprises a deflector to deflect unwanted ions from the ion path.

Claim 90. The TOFMS according to claim 77, wherein said means for generating said ions is selected from the group consisting of fast atom bombardment, matrix assisted laser desorption, plasma desorption, secondary ion generation, and electron bombardment.

Claim 91. The TOFMS according to claim 77, wherein said ions are generated from a sample selected from the group consisting of a protein and DNA.



Claim 92. A method of improving mass resolution in time-of-flight mass spectrometry, said method comprising the steps of:

establishing a first electric field in a source region that includes a sample holder;

ionizing a sample proximately disposed to said sample holder to form sample ions;

establishing a second electric field in an accelerating region;

energizing an ion deflector spaced apart from the first element; and

detecting said sample ions at an ion detector such that mass to charge ratios of said sample ions may be determined;

wherein said first electric field accelerates said sample ions from said sample holder toward said accelerating region;

wherein said second electric field accelerates said sample ions from said sample holder toward said deflector; and

wherein the time spread in the time of flight of said sample ions of a predetermined mass to charge ratio generated within said source region to said ion detector is minimized.

Claim 93. The method according to claim 92, wherein said accelerating region is defined by a pair of parallel conducting electrodes.

Claim 94. The method according to claim 93, wherein said pair of electrodes comprises at least one plate and at least one grid.

Claim 95. The method according to claim 93, wherein at least one potential is applied to at least one of said electrodes to create said second electric field.

Claim 96. The A method according to claim 93, wherein said ions generated in said source region have an initial velocity component parallel to a surface of said electrodes.

Claim 97. The method according to claim 92, wherein said ions have an initial velocity component perpendicular to said sample holder.

Claim 98. The method according to claim 92, wherein said ions are desorbed from a surface of said sample holder.

Claim 99. The A method according to claim 92, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 100. The method according to claim 92, wherein said ions are continuously generated in said source region.

Claim 101. The method according to claim 92, wherein said ions have a initial velocity component.

Claim 102. The method according to claim 92, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 103. The method according to claim 92, wherein said method further comprises the step of deflecting unwanted ions from the ion path.

Claim 104. The method according to claim 92, wherein said ions are generated from a sample selected from the group consisting of a protein and DNA.

Claim 105. A method of operating a time-of-flight mass spectrometer (TOFMS) having a first region including a sample source disposed therein, and flight tube region including an ion detector, said method comprising the steps of:

generating ions from a sample source within the first region;

establishing an ion accelerating field within the flight tube region, said ion accelerating field accelerating said ions generated within the first region toward the ion detector; and

detecting said accelerated ions at the ion detector and determining the mass to charge ratios of said accelerated ions.

Claim 106. The method according to claim 105, wherein said method further comprises the step of energizing an ion deflector remote from said first region such that said ions accelerated by said accelerating field are reflected toward said ion detector.

Claim 107. The method according to claim 105, wherein said ion accelerating field is established across a pair of parallel conducting electrodes.

Claim 108. The method according to claim 107, wherein said pair of electrodes comprises at least one plate and at least one grid.

Claim 109. The method according to claim 107, wherein at least one potential is applied to at least one of said electrodes to create said accelerating field.

Claim 110. The method according to claim 107, wherein said ions generated from said sample source have an initial velocity component parallel to a surface of said electrodes.

Claim 111. The method according to claim 107, wherein said ions have an initial velocity component perpendicular to a surface of said sample source.

Claim 112. The method according to claim 107, wherein said ions are desorbed from a surface of said sample source.

Claim 113. The method according to claim 107, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 114. The method according to claim 107, wherein said ions are continuously generate in said first region.

Claim 115. The method according to claim 107, wherein said ions have a initial velocity component.

Claim 116. The method according to claim 107, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 117. The method according to claim 107, wherein said method further comprises the step of deflecting unwanted ions from the ion path.

Claim 118. The method according to claim 107, wherein said ions are generated from a sample selected from the group consisting of a protein and DNA.

Claim 119. A method of operating a time-of-flight mass spectrometer, the spectrometer having a source region including a sample source disposed therein, an analyzer region including an ion accelerating means and an ion detector positioned remote from the source region, said method comprising the steps of:

establishing a non-zero field within the source region;

generating ions from the sample source within the source region;

establishing an ion accelerating field within the analyzer region after establishing said non-zero field in the source region, said ion accelerating field orthogonally accelerating said ions generated within said source region in a path leading to the ion detector; and

detecting said accelerated ions at the ion detector and determining therefrom mass to charge ratios of said accelerated ions.

Claim 120. The method according to claim 119, wherein said method further comprises the step of energizing an ion deflector remote from said source region such that said ions accelerated by said accelerating field are reflected toward said ion detector.

Claim 121. The method according to claim 119, wherein said ion accelerating field is established across a pair of parallel conducting electrodes.

Claim 122. The method according to claim 121, wherein said pair of electrodes comprises at least one plate and at least one grid.

Claim 123. The method according to claim 121, wherein at least one potential is applied to at least one of said electrodes to create said accelerating field.

Claim 124. The method according to claim 121, wherein said ions generated from said sample source have an initial velocity component parallel to a surface of said electrodes.

Claim 125. The method according to claim 119, wherein said ions have an initial velocity component perpendicular to a surface of said sample source.

Claim 126. The method according to claim 119, wherein said ions are desorbed from a surface of said sample source.

Claim 127. The method according to claim 119, wherein a voltage pulse is applied to said detector to increase the gain of said detector.

Claim 128. The method according to claim 119, wherein said ions are continuously generated in said source region.

Claim 129. The method according to claim 119, wherein said ions have a initial velocity component.

Claim 130. The method according to claim 119, wherein said ions have an average initial velocity distribution not equal to zero.

Claim 131. The method according to claim 119, wherein said method further comprises the step of deflecting unwanted ions from the ion path.

Claim 132. The method according to claim 119, wherein said ions are generated from a sample selected from the group consisting of a protein and DNA.

Claim 133. A method of improving mass resolution in time-of-flight mass spectrometry by compensating for an initial velocity distribution of ions to at least second order comprising:

- a) applying a potential to a sample holder;
- b) applying a potential to a first element spaced apart from the sample holder which, together with the potential on the sample holder defines a first electric field between the sample holder and the first element;
- c) ionizing a sample proximately disposed to the holder to form sample ions;
- d) applying a second potential to either the sample holder or the first element at a predetermined time subsequent to steps a) through c) which together with the potential on the first element, defines a second electric field between the sample holder and the first element, and which extracts the ions from the first element after the predetermined time;
- and
- e) energizing an ion reflector spaced apart from the first element;

wherein the first and second electric fields and the predetermined time are chosen such that a flight time of the extracted ions of like mass-to-charge ratio from the reflector to a detector will be independent to second order of the initial velocity.